

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A chemically modified ~~double stranded short interfering ribonucleic acid (siRNA)~~ molecule comprising a ~~sense strand and an antisense strand~~, wherein:
 - a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;
 - b) each strand of said siRNA nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - c) an 18 to 27 nucleotide sequence of the antisense strand of said siRNA nucleic acid molecule comprises about 18 to about 27 nucleotides that are is complementary to HCV RNA nucleotide sequence comprising SEQ ID NO: 1706; and the sense strand is complementary to the antisense strand;
 - d) an 18 to 27 nucleotide sequence of the sense strand of the siRNA nucleic acid molecule is complementary to the antisense strand and comprises a portion an 18 to 27 nucleotide sequence of the HCV RNA nucleotide sequence of about 18 to about 27 nucleotides; and
 - e) about 50 to 100 percent of the nucleotides positions in one or both strands the sense stand and about 50 to 100 percent of the nucleotides in the antisense strand of the siRNA molecule are chemically modified with modifications independently selected from the group consisting of and the antisense strand of the siRNA molecule comprises about 5, 6, 7, 8, 9, 10 or more 2'-O-methyl nucleotides, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and
 - f) one or more of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2'-O-methyl purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

2-14. (Canceled)

15. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein one 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the pyrimidine nucleotides present in the sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

16. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends of the sense strand.

17. (Currently amended) The siRNA nucleic acid molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.

18. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein one 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

19. (Canceled)

20. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein the antisense strand comprises includes a terminal phosphorothioate internucleotide linkage at the 3' end of said antisense strand.

21-31. (Canceled)

32. (Currently amended) A composition comprising the siRNA nucleic acid molecule of claim 1 in a pharmaceutically acceptable carrier or diluent.

33-35. (Canceled)

36. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein one 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides.

37. (Currently amended) The siRNA nucleic acid molecule of claim 1, wherein one 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the purine nucleotides present in the sense strand are 2'-deoxy purine nucleotides.

38. (Currently amended) The ~~siRNA nucleic acid~~ molecule of claim 1, wherein ~~one~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides.

39. (Currently amended) The ~~siRNA nucleic acid~~ molecule of claim 1, wherein ~~one~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the purine nucleotides present in the antisense strand ~~comprise~~ are 2'-deoxy[[-]] purine nucleotides.

40. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises one or more ribonucleotides.

41. (New) The nucleic acid molecule of claim 1, wherein the 5'-end of said antisense strand includes a terminal phosphate group.

42. (New) The nucleic acid molecule of claim 1, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides.

43. (New) The nucleic acid molecule of claim 1, wherein the antisense strand, sense strand, or both the antisense and sense strand include a 3'-overhang of 1-3 nucleotides.

44. (New) The nucleic acid molecule of claim 43, wherein the nucleotides of the 3'-overhang are chemically modified to comprise one or more phosphorothioate internucleotide linkages, 2'-O-methyl ribonucleotides, 2'-deoxy-2'-fluoro ribonucleotides, 2'-deoxy ribonucleotides, universal base nucleotides, 5-C-methyl nucleotides, inverted deoxyabasic moieties or a combination thereof.

45. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more phosphorothioate internucleotide linkages in the sense strand, the antisense strand, or both the sense strand and the antisense strand.

46. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more 2'-O-methoxyethyl (MOE) nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.

47. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more locked nucleic acid (LNA) nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.

48. (New) A chemically modified nucleic acid molecule comprising a sense strand and a separate antisense strand, wherein:

- a) each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length;
- b) an 18 to 27 nucleotide sequence of the antisense strand of said nucleic acid molecule is complementary to HCV RNA sequence comprising SEQ ID NO: 1706;
- c) an 18 to 27 nucleotide sequence of the sense strand of said nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the HCV RNA sequence;
- d) the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends;
- e) one or more of the nucleotides present in the sense strand and one or more of the nucleotides present in the antisense strand are 2'-O-methyl modified nucleotides; and
- f) one to ten or more of the pyrimidine nucleotides present in the sense strand and one to ten or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

49. (New) A composition comprising the nucleic acid molecule of claim 48 in a pharmaceutically acceptable carrier or diluent.

50. (New) A chemically modified nucleic acid molecule, wherein:

- a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;
- b) each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length;
- c) an 18 to 27 nucleotide sequence of the antisense strand of the nucleic acid molecule is complementary to a HCV RNA sequence comprising SEQ ID NO: 1706;

- d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the HCV RNA sequence;
- e) at least 50% of the nucleotides of each strand of said nucleic acid molecule comprise modified nucleotides having a sugar modification selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, and deoxyabasic modifications;
- f) at least one of said sugar modifications is a 2'-O-methyl modification; and
- g) each strand of said nucleic acid molecule has no more than 3 consecutive ribonucleotides.

51. (New) A composition comprising the nucleic acid molecule of claim 50 in a pharmaceutically acceptable carrier or diluent.

52. (New) A method of modulating the expression of a HCV gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 1 to the cell under conditions suitable for modulating the expression of the HCV gene in the cell.

53. (New) A method of modulating the expression of a HCV gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 50 to the cell under conditions suitable for modulating the expression of the HCV gene in the cell.